REMARKS

Claims 1-6, 8, 12 and 19-24 currently appear in this application. The Office Action of August 9, 2007, has been carefully studied. These claims define novel and unobvious subject matter under sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

The Claimed Invention

The invention claimed herein relates to a method for stabilizing a solution formulation containing a recombinant protein. The characteristic feature of this method is to store the solution under a magnetic field.

The applicant presumes that such stabilization of a recombinant protein solution results from suppressing random collisions between proteins in the solution by maintaining the solution under the influence of a magnetic field. That is, it is considered that, although protein molecules would exist in a disorderly fashion in a solution not subject to a magnetic field, when a magnetic field is applied to the solution, the status of the molecules would change to one that is ordered along the direction of the magnetic field because of the existence of charges in each protein molecule. This change in

status of the protein molecules in solution reduces collisions between the molecules, and thereby stabilizes the protein formulation.

Election/Restriction

It is noted with appreciation that claim 6 will be rejoined since it is not burdensome to search these additional species.

Art Rejections

Claims 1, 3, 4, 11, 12, 19-21 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Bohr et al., U.S. 6,060,293.

This rejection is respectfully traversed. It is respectfully submitted that Bohr does not teach a method for stabilizing a recombinant protein solution under the influence of a magnetic field. Rather, Bohr relates to applying electromagnetic radiation such as microwaves to chain molecules such as proteins to change the structure of the molecule. This has nothing to do with stabilizing a recombinant protein solution by subjecting the solution to the influence of a magnetic field.

There is nothing in Bohr that teaches or suggests that a recombinant protein solution formulation is stored under a magnetic field so as to stabilize the formulation. On

the contrary, Bohr discloses that a three-dimensional structure of a chain molecule such as a protein can be **changed** by applying energy from a high frequency energy source such as microwaves and radio waves to the molecules (see, for example, abstract and column 3, line 66- column 4, line 15). In other words, Bohr discloses applying radiation having high frequency energy, such as microwaves, to a chain molecule to rotate or vibrate an amino acid residue contained in the molecule, whereby the three-dimensional structure of the molecule is changed.

Moreover, it is respectfully submitted that the application of high frequency energy as disclosed in Bohr would not necessarily stabilize a protein molecule. Bohr discloses **changing** the structure of a three-dimensional molecule, while the method claimed herein is concerned with **stabilizing** a protein molecule.

It is respectfully submitted that microwave radiation, as disclosed by Bohr, acts to destabilize protein molecules, in contrast with the presently claimed method that uses a magnetic field to stabilize protein molecules.

Submitted herewith are copies of the following:

Zhong et al., *Nature Biotechnology* **22(2)**: 1291-1296 (2004)

Milestone, "Microwave Protein Hydrolysis."

In the above two articles, microwave irradiation is used to decompose a protein molecule, for example, Zhong et al. shows that microwave irradiation can promote protein hydrolysis (please see the abstract of the article). It is respectfully submitted that the promotion of protein hydrolysis may partly result from conformational or structural changes of a protein under microwave irradiation, leading to destabilization of the protein (refer to page 1291, right column, lines 15-16). Accordingly, it is respectfully submitted that the effect of a magnetic field on a protein molecule in solution is different from that of electromagnetic high frequency radiation such as microwaves.

Moreover, although the Examiner asserts that the method of Bohr is to stabilize a protein solution, it is respectfully submitted that Bohr is silent regarding stabilization of a solution. Moreover, Bohr merely states that the application of high frequency energy changes the three-dimensional structure of a protein molecule. Thus, it is respectfully submitted that the technical feature of the present invention is entirely different from that of Bohr.

Claims 1-6, 11, 12 and 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bohr as applied above, and further in view of the rationale below with support from Plantanias et al., *Journal of Clinical Oncology* 9:2021-

2026, 1991 and Rosse et al., *Hematology* 2000, 2-18. The Examiner concedes that Bohr dose not specifically teach storage of recombinant hematopoietic factors such as erythropoietin and granulocyte colony-stimulating factor. Plantanias and Rosse are said to teach that recombinant molecules have been used as therapeutic agents.

This rejection is respectfully traversed. As noted above, there is nothing in Bohr that teaches or suggests stabilizing a protein in solution using magnetic energy. Bohr teaches using high frequency electromagnetic energy to **destabilize** proteins. It is immaterial whether the proteins of Bohr can be used as therapeutics, because the Bohr proteins are not stabilized. It is only in the presently claimed process that the proteins are stabilized.

There is nothing in Bohr that teaches or suggests that a magnetic field can stabilize any type of protein solution. Bohr only teaches using high frequency electromagnetic energy to change protein conformation, that is, to **destabilize** the proteins.

Claims 1-6, 8, 11, 12 and 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bohr as applied above, and further in view of Cohen et al., U.S. 3,308,809. The Examiner asserts that claim 8 recites storing the stabilized protein solution in a syringe, and that Cohen

discloses using a syringe to store blood specimens from humans.

This rejection is respectfully traversed. As noted above, Bohr teaches destabilizing proteins by changing their three-dimensional structures. Cohen merely discloses storing blood products in a syringe.

It is not understood why this rejection was made to claims other than claim 8, as claim 8 is the only claim that recites that the formulation is stored in a syringe. Moreover, Cohen merely describes using a syringe to withdraw blood from a human and then to dispense the blood for analysis. It is respectfully submitted that it is a far stretch to analogize recombinant protein to whole blood, and to equate a syringe used for storage and treatment to a syringe used for withdrawal and subsequent dispensing.

There is nothing in Bohr, either alone or in combination with any of the other cited references, that would lead one skilled in the art to store proteins under a magnetic field in order to stabilize the proteins, because Bohr specifically teaches using high frequency electromagnetic waves to change the proteins' configuration, *i.e.*, to destabilize the proteins.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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